In the Claims

Please cancel claims 1-89, without prejudice to applicant's right to pursue the subject matter thereof in a continuing application.

Please add new claims 90-163 as follows:

90. (New) A method for detecting the presence or absence of a mutation characterized by the presence of a predefined nucleotide at a predefined position in a nucleic acid molecule which comprises:

(a) contacting the nucleic acid molecule with a probe comprising a first and a second nucleic acid segment, the 5' end of the first segment being covalently linked to the 3' end of the second segment, wherein either (a) the nucleotide at the 5' end of such second segment is complementary to the predefined nucleotide or (b) the nucleotide at the 3' end of such first segment is complementary to the predefined nucleotide, under conditions such that the probe hybridizes with the nucleic acid molecule;

(b) contacting the hybridized product from step (a) with a ligase under conditions such that the unlinked ends of the segments ligate together if the nucleic acid molecule contains the mutation, and

(c) determining whether the unlinked ends of the segments

have ligated together, so as to thereby detect the presence or absence of the mutation in the nucleic acid molecule

91. (New) The method of claim 90, wherein the nucleic acid molecule is a DNA molecule.

92. (New) The method of claim 90, wherein the nucleic acid molecule is an RNA molecule.

93. (New) The method of claim 90, wherein the nucleic acid molecule is a mitochondrial DNA molecule.

94. (New) The method of claim 90, wherein the nucleic acid molecule is a chromosomal DNA molecule.

95. (New) The method of claim 90, wherein the nucleic acid molecule is a viral DNA molecule.

96. (New) The method of claim 90, wherein the nucleic acid molecule is a cDNA molecule.

97. (New) The method of claim 90, wherein the probe segments comprise nucleotides modified in their sugar, phosphate or base.

98. (New) The method of claim 97, wherein the modified nucleotide is a phosphorothioate, phosphoramidate, phosphorodithioate, peptide nucleic acid, phosphonate, methylphosphonate or phosphate ester.

99. (New) The method of claim 90, wherein the two probe segments are covalently linked by an oligonucleotide.

100. (New) The method of claim 90, wherein the probe is labeled with a detectable moiety.

101. (New) The method of claim 100, wherein the detectable moiety is a florescent label, a radioactive atom, a chemiluminescent label, a paramagnetic ion, biotin or a label which can be detected through a secondary enzymatic or binding step.

102. (New) The method of claim 90, wherein the determination is by means of an enzymatic reaction selection method.

103. (New) The method of claim 90, wherein the determination is by means of a fluorescence selection method.

104. (New) The method of claim 90, wherein the determination is by means of a chemiluminescence selection method.

105. (New) The method of claim 90, wherein the determination is by means of a magnetic charge selection method.

106. (New) The method of claim 90, wherein the probe is attached to a solid support.

107. (New) The method of claim 90, wherein the nucleic acid molecules are attached to a solid support.

108. (New) The method of claim 90, wherein the nucleic acid molecule is circular and ligation of the unlinked ends results in catenation.

109. (New) The method of claim 90, wherein the mutation(s) is a point mutation.

110. (New) The method of claim 90, wherein the mutation(s) is a deletion mutation.

111. (New) The method of claim 90, wherein the mutation(s) is an insertion mutation.

112. (New) The method of claim 90, wherein the mutation(s) is a translocation mutation.

113. (New) The method of claim 90, wherein the mutation(s) is an inversion mutation.

114. (New) The method of claim 90, wherein the nucleic acid molecule contains a plurality of detectable mutations.

115. (New) A method for detecting the presence or absence of a predefined mutation characterized by the presence of a predefined nucleotide at a predefined position in a nucleic acid molecule associated with a genetic disorder in a subject which comprises:

(a) contacting a sample of bodily fluid or tissue from the

subject containing the nucleic acid molecule associated with the genetic disorder, with a probe comprising a first and a second nucleic acid segment, the 5' end of the first segment being covalently linked to the 3' end of the second segment, wherein either (a) the nucleotide at the 5' end of such second segment is complementary to the predefined nucleotide or (b) the nucleotide at the 3' end of such first segment is complementary to the predefined nucleotide, under conditions such that the probe hybridizes with the nucleic acid molecule;

(b) contacting the hybridized product from step (a) with a ligase under conditions such that the unlinked ends of the segments ligate together if the nucleic acid molecule contains the predefined mutation associated with the genetic disorder, and

(c) determining whether the unlinked ends of the segments have ligated together, so as to thereby detect the presence or absence of the predefined mutation associated with the genetic disorder in the subject

116. (New) The method of claim 115, wherein the nucleic acid molecule(s) is covalently linked to a solid support.

117. (New) The method of claim 115, wherein the probe(s) is covalently linked to a solid support.

118. (New) The method of claim 115 or 116, wherein the solid

support is a microscope slide comprised of plastic or glass, either uncoated or coated with a suitable attachment substrate.

119. (New) The method of claim 115 or 116, wherein the solid support is a nylon membrane, a cellulose acetate membrane, an epoxy-activated synthetic copolymer membrane or a nitrocellulose membrane.

120. (New) The method of claim 115 or 116, wherein the solid support is a tube or bead or any part thereof, which is sepharose, latex, glass or plastic.

121. (New) The method of claim 115, wherein the probe is labeled with a detectable moiety.

122. (New) The method of claim 121, wherein the detectable moiety is a fluorescent label, a radioactive atom, a chemiluminescent label, a paramagnetic ion, biotin or a label which can be detected through a secondary enzymatic or binding step.

123. (New) The method of claim 115, wherein the determination is by means of an enzymatic reaction selection method.

124. (New) The method of claim 115, wherein the determination is by means of a fluorescence selection method.

125. (New) The method of claim 115, wherein the determination is

by means of a chemiluminescence selection method.

126. (New) The method of claim 115, wherein the determination of the presence or absence of bound nucleic acid molecule(s) is by means of a magnetic charge selection method.

127. (New) The method of claim 115, wherein the nucleic acid molecules are attached to a solid support.

128. (New) The method of claim 115, wherein the nucleic acid molecule is circular and ligation of the unlinked ends results in catenation.

129. (New) The method of claim 115, wherein the genetic disorder is associated with a point mutation.

130. (New) The method of claim 115, wherein the genetic disorder is associated with a deletion mutation.

131. (New) The method of claim 115, wherein the genetic disorder is associated with an insertion mutation.

132. (New) The method of claim 115, wherein the genetic disorder is associated with a translocation mutation.

133. (New) The method of claim 115, wherein the genetic disorder is associated with an inversion mutation.

134. (New) The method of claim 115, wherein the nucleic acid

molecule contains a plurality of detectable genetic disorders.

135. (New) A method for identifying the presence or absence of a predefined neutral polymorphism characterized by the presence of a predefined nucleotide at a predefined position in a nucleic acid molecule in a subject which comprises:

(a) contacting a sample of bodily fluid or tissue from the subject containing the nucleic acid molecule associated with the neutral polymorphism, with a probe comprising a first and a second nucleic acid segment, the 5' end of the first segment being covalently linked to the 3' end of the second segment, wherein either (a) the nucleotide at the 5' end of such second segment is complementary to the predefined nucleotide or (b) the 3' end of such first segment is complementary to the predefined nucleotide, under conditions such that the probe hybridizes with the nucleic acid molecule;

(b) contacting the hybridized product from step (a) with a ligase under conditions such that the unlinked ends of the segments ligate together if the nucleic acid molecule contains the neutral polymorphism, and

(c) determining whether the unlinked ends of the segments have ligated together, so as to identify the presence or absence of the predefined neutral polymorphism in the

subject.

136. (New) A method for selecting a particular mutation in a nucleic acid molecule from a population of engineered nucleic acid molecules containing random mutations, which comprises:

(a) contacting a sample containing the nucleic acid molecule which may contain the particular mutation, with a probe comprising a first and a second nucleic acid segment, the 5' end of the first segment being covalently linked to the 3' end of the second segment, wherein either (a) the nucleotide at the 5' end of such second segment is complementary to the predefined nucleotide or (b) the nucleotide at the 3' end of such first segment is complementary to the predefined nucleotide, under conditions such that the probe hybridizes with the nucleic acid molecule;

(b) contacting the hybridized product from step (a) with a ligase under conditions such that the unlinked ends of the segments ligate together if the nucleic acid molecule contains the particular mutation, and

(c) determining whether the unlinked ends of the segments have ligated together, so as to thereby select the nucleic acid molecule containing the particular mutation from the population of engineered nucleic acid molecules.

137. (New) The method of claim 136, wherein the nucleic acid molecule is covalently linked to a solid support.

138. (New) The method of claim 136, wherein the probe is covalently linked to a solid support.

139. (New) The method of claim 137 or 138, wherein the solid support is a microscope slide comprised of plastic or glass.

140. (New) The method of claim 137 or 138, wherein the solid support is a nylon or nitrocellulose membrane.

141. (New) The method of claim 137 or 138, wherein the solid support is a bead which is sepharose, latex, glass or plastic.

142. (New) The method of claim 136, wherein the probe is labeled with a detectable moiety.

143. (New) The method of claim 142, wherein the detectable moiety is a florescent label, a radioactive atom, a chemiluminescent label, a paramagnetic ion, biotin or a label which can be detected through a secondary enzymatic or binding step.

144. (New) The method of claim 136, wherein the selection is by means of an enzymatic reaction selection method.

145. (New) The method of claim 136, wherein the selection is by means of a fluorescence based selection method.

146. (New) The method of claim 136, wherein the selection is by means of a chemiluminescence based selection method.

147. (New) The method of claim 136, wherein the selection is by means of magnetic charge based selection method.

148. (New) The method of claim 136, wherein the nucleic acid molecules are attached to a solid support.

149. (New) The method of claim 136, wherein the nucleic acid is circular and ligation of the unlinked ends results in catenation.

150. (New) The method of claim 136, wherein the particular mutation is associated with a point mutation.

151. (New) The method of claim 136, wherein the particular mutation is associated with a deletion mutation.

152. (New) The method of claim 136, wherein the particular mutation is associated with an insertion mutation.

153. (New) The method of claim 136, wherein the particular mutation is associated with an inversion mutation.

154. (New) A method for detecting the presence or absence of a

mutation characterized by the presence of a predefined nucleotide at a predefined position in a circular DNA molecule which comprises:

(a) contacting the circular DNA molecule with a probe comprising a first and a second nucleic acid segment, the 5' end of the first segment being covalently connected to the 3' end of the second segment, wherein the 5' end of the second segment or the 3' end of the first segment is complementary to the predefined nucleotide, under conditions such that the probe hybridizes with the circular DNA molecule;

(b) contacting the hybridization product from step (a) with a ligase under conditions such that the unlinked ends of the first and second segments ligate together only if the circular DNA molecule contains the predefined nucleotide mutation, and

(c) determining whether the unlinked ends of the first and second segments have ligated together, so as to thereby detect the presence or absence of the mutation in the circular DNA molecule.

155. (New) The method of claim 154, wherein the covalent connection of the probe ends is performed by enzymatic ligation.

156. (New) The method of claim 154, wherein the target molecule

is a cDNA or an RNA sequence.

157. (New) The method of claim 154, wherein the probe is an oligonucleotide.

158. (New) The method of claim 154, wherein the segment or segments are selected from polypeptide, hydrocarbon linker, poly-propylene glycol, or poly-phosphate linker.

159. (New) The method of claim 154, wherein the probe or probes are immobilized to a solid support.

160. (New) The method of claim 154, wherein the target sequence is immobilized to a solid support.

161. (New) The method of claim 154, wherein the sample is a population of engineered nucleic acid molecules.

162. (New) A method of detecting a target molecule having a defined nucleic acid sequence in a sample which comprises:

(a) providing a detectable probe with two free nucleic acid end parts which are complementary to at least a part of, and capable of hybridizing to, two regions of the target molecule, and

(b) hybridizing the probe ends to the target molecule under hybridizing conditions.

(c) covalently connecting the ends of the hybridized probe with each other to form a circularized structure which binds the target molecule through catenation,

(d) subjecting the target molecule to denaturing conditions to release any non-circularized probe from the target molecule, thereby retaining only the circularized probe bound to the target molecule, and

(e) detecting the presence of catenated probe, as indicative of the presence of the target molecule of defined nucleic acid sequence thus detecting the target nucleic acid in the sample.

163. (New) A method of selectively capturing a target molecule having a defined nucleic acid sequence on a solid support which comprises:

(a) providing a probe with two free nucleic acid end parts which are complementary to at least a part of and capable of hybridizing to two regions of the target molecule, said probe being immobilized to the solid support,

(b) hybridizing the probe ends to the target molecule under hybridizing conditions,

(c) covalently connecting the ends of the hybridized probe with each other to form a circularized structure which binds with the target molecule through catenation, and

(d) subjecting the support with the captured target molecule to denaturing conditions to release any non-catenated target molecule from the support so as to selectively capture a target molecule with a defined nucleic acid sequence.